

# Small in-stent Low Density on CT Angiography after Carotid Artery Stenting

MIKA OKAHARA<sup>1</sup>, HIRO KIYOSUE<sup>2</sup>, JUNJI KASHIWAGI<sup>1</sup>, SHINYA UEDA<sup>1</sup>, YUZO HORI<sup>3</sup>, HIROMU MORI<sup>2</sup>

<sup>1</sup> Department of Radiology, Shinbeppu Hospital

<sup>2</sup> Department of Radiology, Oita University Faculty of Medicine,

<sup>3</sup> Department of Radiology, Nagatomi Neurosurgical Hospital

**Key words:** carotid stenosis, stenting, CAS

## Summary

Carotid stenting (CAS) for carotid stenosis has developed rapidly over the last decade. In-stent low density area supposed plaque protrusion or thrombus is sometimes observed on CT angiography after CAS. We evaluate the frequency and time course of the small in-stent low density after carotid artery stenting and discuss its nature and clinical significance.

Between May 2005 to November 2007, 23 CASs were performed for 20 patients with carotid artery stenosis. All patients had no in-stent defect on digital subtraction angiography (DSA) immediately after the procedure. Follow-up CT angiography was performed at seven 7-10 days, 1-2 months, 6 months, and then every 6 months following CAS. We retrospectively reviewed the follow-up CT angiographic findings and clinical ischemic events.

Small in-stent low density areas on CT angiography were observed in 6 lesions (26%). Four cases were added warfarin to antiplatelets and the other two cases had antiplatelets only. The in-stent low density areas were disappeared within four months after CAS and no ischemic event was observed in five patients.

In the other patient, a small in-stent low density area had decreased at one month after CAS, but another small in-stent low density area appeared at five months.

Subacute small in-stent low density areas were frequently observed on CT angiography follow-

ing CAS, however, the low density area will disappear without clinical events by medication in most case.

## Introduction

Carotid artery stenting (CAS) has developed rapidly over the last decade as a minimally invasive alternative to carotid endarterectomy (CEA) for extracranial carotid artery stenosis<sup>1-4</sup>. Acute or subacute in-stent thrombosis is a rare but potentially devastating complication following CAS<sup>5-7</sup>. We experienced the patient who had major stroke because of subacute in-stent thrombosis one week after CAS in early chronological series before 2004. We perform follow-up CT angiography at 7-10 days after CAS. Asymptomatic small in-stent low density areas supposed plaque protrusion or thrombus are sometimes observed on CT angiography after CAS. However, there is no report regarding these small in-stent low density areas after CAS to our knowledge. We investigate the frequency and time course of small in-stent low density areas after carotid artery stenting and discuss their nature and clinical significance.

## Materials and Method

Between May 2005 to November 2007, 23 CASs were performed for 20 patients (16 males and 4 females, mean age 72.1 years, ranged 60-80) with cervical carotid artery stenosis.



Two cases (case 7 and 16) were performed CAS for bilateral carotid stenosis and one (case 11) were performed CAS for primary stenosis and re-stenosis.

All patients were given antiplatelets [aspirin (100 mg) and ticlopidine (200 mg), cilostazol (200 mg), or clopidogrel (75 mg)] beginning at least three days before the intervention. Three cases were given warfarin added to the antiplatelets because of transient ischemic attack or chronic atrial fibrillation. Techniques of CAS, including the protection device, size and kinds of stents and angioplasty balloon, were mainly planned based on findings of cervical and intracranial CT angiography.

All CAS procedures were performed by transfemoral approach with local anesthesia.

Intravenous heparin was given to maintain an activated clotting time around 300 sec. throughout the procedure. A 6F, 90cm shuttle sheath (Cook, Bloomington, USA) was placed in the distal common carotid artery (CCA) with a coaxial system using 4F JB2 catheter. Guard-wire (Medtronic, Inc, USA) embolic protection device was used in 18 patients. Filterwire (Mintcatch; Century medical, Inc, Tokyo, Japan) was used for some five patients who were guessed to be intolerable for temporary internal carotid arterial occlusion. A 0.014-inch guidewire system with protection balloon or filter was manipulated to cross the carotid stenosis. After the activation of the embolic protection devices, a monorail angioplasty balloon with 3-3.5 mm diameter

balloon was used to predilate the carotid lesion if necessary. Next, a self expandable stent (SMARTer, Precise [Johnson & Johnson, USA] or Wallstent RP [Boston Scientific, USA]) was deployed across the carotid stenosis. Poststenting balloon angioplasty was performed with monorail angioplasty balloon of the almost same size of just distal internal carotid artery from stenotic lesion.

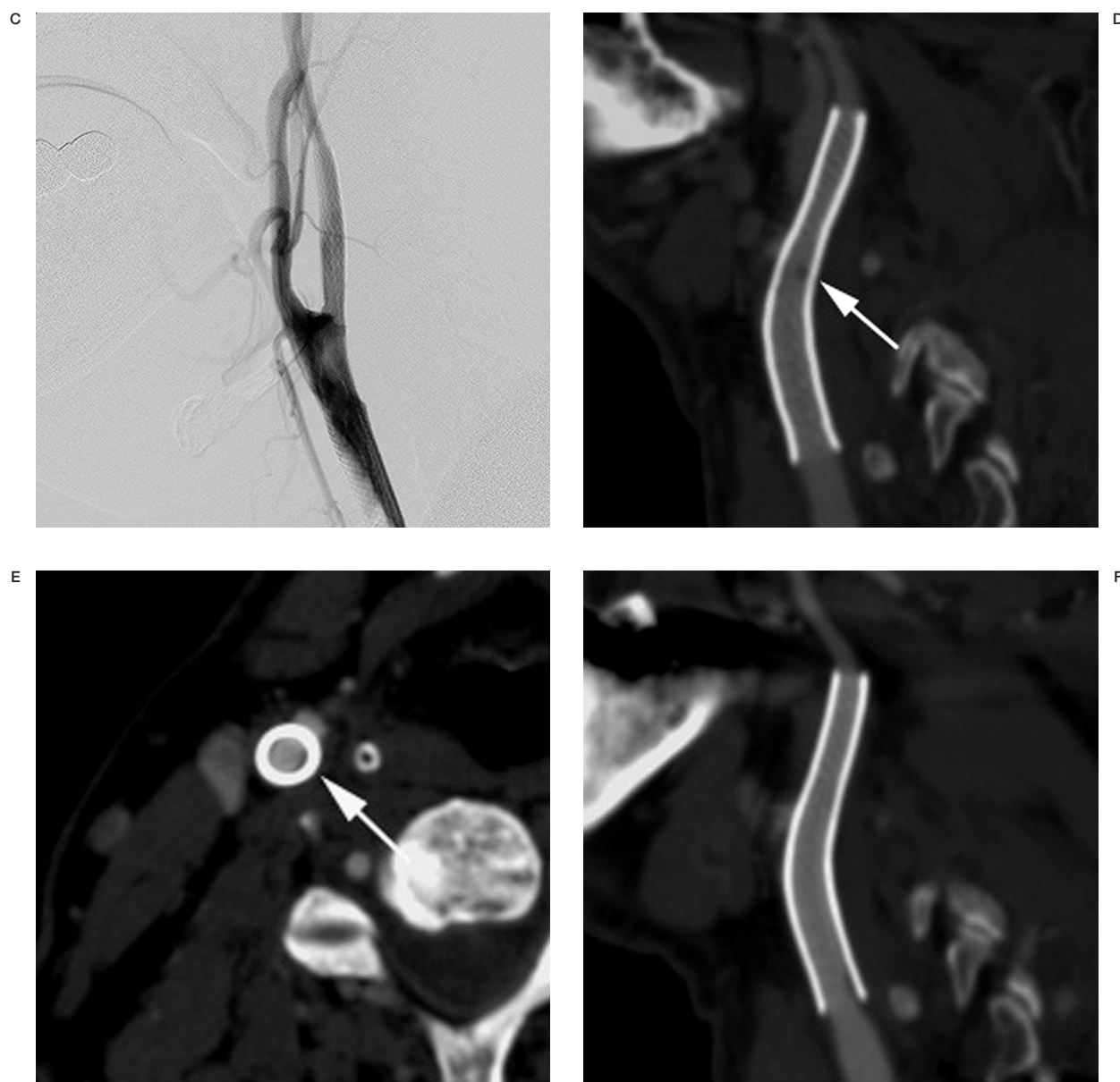
All cases had no in-stent defect on DSA immediately after the procedure.

Follow-up CT angiography was performed at 7-10 days, 1- 2 months, 6 month, and then every six months following CAS. If in-stent low density area remained on follow-up CT 2 months after CAS, additional follow-up CT was performed at 4 month after CAS.

We retrospectively reviewed the follow-up CT angiographic findings and clinical ischemic events. Factors potentially affecting the occurrence of in-stent low density area, including ulcerated lesion before CAS, hypoechoic plaque, and stent types (open cell design or closed cell design) were also assessed. A Yates 2x2 Chi square test was performed. Test results were considered significant at a  $P < 0.05$ .

## Results

Imaging findings before the procedure and technical details are summarized in Table 1. No neurological complication was observed during the procedures and perioperative periods.



**Figure 1** Case 3: 71-year-old male presented with cerebral infarction. Curved planner reconstruction (CPR) of preprocrural CTA (A), and a lateral view of right carotid arteriogram (B) shows severe stenosis with ulceration of right carotid artery. On a lateral view of a right carotid arteriogram (C) immediately after CAS, no in stent filling defect is seen. On CTA (D,E) 7 days after CAS, small in-stent low density area is seen. This patient was observed with antiplatelets only. The small low density area decreased on CTA one month after CAS, and disappeared on CTA three months after CAS.

Small in-stent low density areas were observed in 6 lesions (26%) on the initial follow-up CT angiography. Factors potentially affecting the development of in-stent low density areas are summarized in Table 2.

In the following factors, symptomatic lesion, coexistence of diabetes mellitus and techniques of CAS including stent design, and use of

pre/post balloon dilatation, there were no differences in frequency between the 6 cases developing in-stent low density areas (in-stent low density group) and the other cases without in-stent low density areas. The other factors, including coexistence of ischemic heart disease and hyperlipidemia, presence of ulcerated lesion, and hypoechoic plaque, were more fre-

quently seen in the in-stent low density group. However, there were no statistical significant differences between the both groups.

Ulceration had been observed in 4 (66.7%) of 6 cases developing in-stent low density area on preprocedural CT. On the other hand, it was found in 4 (23.5%) of 17 cases without in-stent low density. Four cases in small in-stent low density areas group were able to be assessed by carotid ultrasonography, and three of four cases (75%) had hypoechoic plaque (soft plaque).

Of the lesions without in-stent low density area, 13 cases were able to be assessed by carotid ultrasonography, and three (23%) had hypoechoic plaque. Six lesions couldn't be sufficiently assessed because of severe long segment stenosis and/or marked calcification.

Four cases were added warfarin to antiplatelets and other two cases (Figure 1) had antiplatelets only. No ischemic event was observed in the 6 patients during 7-23 months follow-up periods (mean 19.6). The in-stent low

Table 1 **Imaging findings / Technical characteristics.**

Lesion No	Patient No	Pre CT Ulceration	US	Follow CT Small in-stent LDA	Types of STENT	Pre PTA	Post PTA
1	1	–	NA	+	SMARTer	+	+
2	2	+	NA	+	Wall RP	+	+
3	3	+	hypo	+	Wall RP	+	+
4	4	+	iso	+	Precise	–	+
5	5	–	hypo	+	Precise	+	+
6	6	+	hypo	+	Precise	–	+
7	7	+	hyper	–	SMARTer	–	–
8		–	hyper	–	Precise	+	+
9	8	+	hyper	–	Wall RP	+	+
10	9	–	hypo	–	Wall RP	–	+
11	10	–	hyper	–	Precise	+	+
12	11	–	hypo	–	Wall RP	+	+
13		–	iso	–	Wall RP	–	+
14	12	+	iso	–	Wall RP	+	+
15	13	+	iso	–	Precise	–	+
16	14	–	NA	–	Precise	–	+
17	15	–	hypo	–	Precise	+	+
18	16	–	NA	–	Wall RP	+	+
19		–	NA	–	Precise	+	+
20	17	–	hyper	–	Precise	+	–
21	18	–	hyper	–	Precise	+	+
22	19	–	–	–	Wall RP	–	+
23	20	–	iso	–	Wall RP	+	+

US: Ultrasonography, LDA: low density area, PTA: percutaneous transarterial angioplasty

density areas were disappeared within four months after CAS. In the other one patient, small in-stent low density area was decreased at 1 month after CAS, but another small in-stent low density area was appeared at five months.

## Discussion

CEA is the gold standard treatment for patient with high-grade carotid artery stenosis and its efficacy has been clearly documented in numerous previous reports<sup>8-12</sup>. However, it has been reported that CAS with distal protection device performed similarly to the CEA for a limited group of CEA high-risk patients<sup>2,13-15</sup>. Because of its less invasiveness and high success rates, CAS has become an alternative to CEA for this subgroup.

Complications of CAS include intraoperative distal embolic event, arterial dissection, carotid sinus reaction, delayed embolism and hyperperfusion syndrome. Acute/subacute in-stent occlusion/stenosis resulting from plaque protrusion and thrombus is a rare but serious complication following CAS.

Asymptomatic small in-stent low density areas are sometimes observed on early follow-up CT angiography after CAS. In this study, small in-stent low density areas were observed in six

lesions (26%). The in-stent low density areas would probably had represented a small plaque protrusion or an in-stent thrombus; however, it is difficult to identify whether it is plaque protrusion or thrombus.

In the coronary interventions, many reports of pathological changes after angioplasty or stenting have been published<sup>16,17</sup>. Early after stenting, fibrin, platelets, and acute inflammatory cells are nearly always present in association with stent struts. Plaque is compressed by the stent struts, and penetration of the stent struts into a lipid core is commonly observed<sup>16</sup>. In the present study, four of six lesions developing small in-stent low density areas that showed ulceration before CAS, and three of four lesions had hypoechoic plaque supposed lipid rich plaque. Although there is no statistical significance, the ulcerated and/or hypoechoic lesions were more frequently seen in cases developing small in-stent low density areas. In cases using open cell design stents, CT showed small round in-stent low density area protruded through the open area between the struts. It was assumed that small in-stent low density area consist mainly of plaque protrusion. In carotid artery stenting, a self-expandable stent is used.

Clark et Al, using serial intravascular ultrasound imaging, reported that self-expandable stents deployed in carotid arteries continue to

Table 2 Potentially risk factor of small in-stent low density area.

Factor	Small in-stent low density area		P value
	+(n=6)	-(n=17)	
Symptomatic	5 (83.3%)	9 (52.9%)	0.40
DM	3 (50.0%)	5 (29.4%)	0.68
IHD	4 (66.7%)	3 (17.6%)	0.08
HL	5 (83.3%)	7 (41.2%)	0.19
Ulceration	4 (66.7%)	4 (23.5%)	0.15
US (hypoechoic plaque)	3/4 (75%)	3/13 (23.0%)	0.19
STENT(open cell type)	4 (66.7%)	9 (52.9%)	1
Pre PTA	4 (66.7%)	11 (64.7%)	1
post PTA	6 (100%)	15 (88.2%)	0.97
DM: diabetes mellitus, IHD: ischemic heart disease, HL: hyperlipidemia, US: ultrasonography, PTA: percutaneous transluminal angioplasty			

enlarge along their entire length<sup>18</sup>. Soft plaque may protrude into the stent a few days after CAS, even if no plaque protrusion has been observed immediately after CAS. Plaque protrusion seems to occur less frequently with closed cell design stents rather than the open cell design stents. However in our study, small in-stent low density areas were observed in two lesions used closed cell design stents (Wallstent RP). This would suggest that the mesh of all stents currently in use cannot completely push out the soft plaque.

In most cases, these small low density areas were disappeared by medication (antiplatelets and anticoagulant). However, it is supposed

that relatively large amount of plaque protrusion into the stent can cause thrombus formation and subacute in-stent thrombosis. Any small low density area should be carefully followed up with warfarin added to antiplatelets. Minute low density area may disappear by antiplatelets only.

## Conclusions

Subacute small in-stent low density areas were frequently observed on CT angiography following CAS. The small low density areas will disappear without clinical events by medication in most case.

## References

- 1 Yadav JS, Roubin GS et Al: Elective stenting of the extracranial carotid arteries. *Circulation* 95: 376-381, 1997.
- 2 Veith FJ, Amor M et Al: Current status of carotid bifurcation angioplasty and stenting based on a consensus of opinion leaders. *J Vasc Surg* 33: 111-116, 2001.
- 3 Ouriel K, Yadav J, Green R: Standards of practice: carotid angioplasty and stenting. *J Vasc Surg* 39: 916-917, 2004.
- 4 Rabe K, Sievert H: Carotid artery stenting: state of the art. *J Interv Cardiol* 17: 417-426, 2004.
- 5 Chaturvedi S, Sohrab S, Tselis A: Carotid stent thrombosis Report 2 fatal cases. *Stroke* 32: 2700-2702, 2001.
- 6 Setacci C, de Donato G et Al: Surgical management of acute carotid thrombosis after carotid stenting: a report of three cases. *J Vasc Surg* 42(5): 993-996, 2005.
- 7 Kurisu K, Manabe H, Ihara T: Case of symptomatic subacute in-stent thrombosis after carotid angioplasty and stenting for severe carotid stenosis. *No Shinkei Geka*. 35(10): 1001-1005, 2007. Japanese.
- 8 Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 325: 445-453, 1991.
- 9 Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 351: 1379-1387, 1998.
- 10 Barnett HJ, Taylor DW et Al: Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 339: 1415-1425, 1998.
- 11 Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 273: 1421-1428, 1995.
- 12 Hobson RW 2<sup>nd</sup>, Weiss DG et Al: Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med* 328: 221-227, 1993.
- 13 Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (Cavatas) a randomised trial. *Lancet* 357: 1729-1737, 2001.
- 14 In: JS Yadav, Editor, Carotid stenting in high-risk patients design and rationale of the Sapphire trial, *Cleve Clin J Med* 71 (Sup 1): S45-S46, 2004.
- 15 Lin PH, Bush RL et Al: Carotid artery stenting with routine cerebral protection in high-risk patients. *Am J Surg* 188: 644-652, 2004.
- 16 Farb A, Sangiorgi G et Al: Pathology of acute and chronic coronary stenting in humans. *Circulation* 99: 44-52, 1999.
- 17 Farb A, Burke AP et Al: Pathological mechanisms of fatal late coronary stent thrombosis in humans 108: 1701-1706, 2003.
- 18 Clark DJ, Lessio S et Al: Mechanism and predictors of carotid artery atent restenosis; a serial intravascular ultrasound study 47: 2390-2396, 2006.

Mika Okahara, M.D.  
Department of Radiology  
Shinbeppu Hospital  
3898 Tsurumi, Beppu, 874-0833  
JAPAN  
E-mail: okahara@med.oita-u.ac.jp